

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently amended) A method for the preparation of ~~microsphere~~ microspheres, which comprises the following steps:

(a) emulsifying a medicament-containing polymer solution containing a medicament, a biocompatible and biodegradable hardly-water-soluble polymer and an organic solvent having a boiling point lower than that of water into an aqueous solution in an emulsifying device to form an emulsion wherein said medicament-containing polymer solution is dispersed in the aqueous solution;

(b) transferring the obtained emulsion into a microsphere storage tank;

(c) introducing a part of the emulsion from the microsphere storage tank into a cross flow filter;

(d-1)-i) returning a liquid passing over the cross flow filter to the microsphere storage tank;

(d-1)-ii) recycling a filtrate filtered from the above cross flow filter as an aqueous solution for **[[Step]]** step (a), repeating **[[Steps]]** steps (a) to (d-1), and when the organic solvent having a boiling point lower than that of water is immiscible with water, then evaporating said organic solvent in the microsphere storage tank during this circulation process; or

(d-2)-i) returning a liquid passing over the cross flow filter to the microsphere storage tank;

(d-2)-ii) discharging a filtrate filtered from the above cross flow filter without recycling it as the aqueous solution for ~~[[Step]]~~ step (a), repeating ~~[[Steps]]~~ steps (a) to (d-2) ~~[[with]]~~ using a fresh aqueous solution, and when the organic solvent having a boiling point lower than that of water is immiscible with water, then evaporating said organic solvent in the microsphere storage tank during this circulation process; and

(e) collecting ~~microsphere~~ microspheres in the microsphere storage tank after ~~[[Step]]~~ step (d-1) or step (d-2) is completed.

2. (Currently amended) The method according to claim 1, wherein the medicament-containing polymer solution is one of the following ~~[[ones]]~~:

(i) a solution in which a biocompatible and biodegradable hardly-water-soluble polymer and a medicament are dissolved in an organic solvent having a boiling point lower than that of water;

(ii) a suspension in which a biocompatible and biodegradable hardly-water-soluble polymer is dissolved in an organic solvent having a boiling point lower than that of water, and a medicament is suspended in the resulting polymer solution;

(iii) a dispersion in which a biocompatible and biodegradable hardly-water-soluble polymer is dissolved in an organic solvent having a boiling point lower than that of water, and an aqueous solution of medicament is dispersed in the resulting polymer solution; and

(iv) a dispersion in which one of biocompatible and biodegradable hardly-water-soluble polymers is dissolved in an organic solvent having a boiling point lower than that of water, and a solution of the other biocompatible and biodegradable

hardly-water-soluble polymer in the same organic solvent is dispersed in the resulting polymer solution, and further a medicament is dissolved or suspended in the dispersed polymer solution.

3. (Currently Amended) The method according to claim 1, wherein the emulsification of **[[Step]]** step (a) is carried out continuously, and the resulting emulsion is transferred continuously into the microsphere storage tank.

4. (Currently Amended) The method according to claim 1, wherein the emulsification of **[[Step]]** step (a) is carried out by batch-treatment, and the resulting emulsion in each batch is transferred individually into the microsphere storage tank.

5. (Previously presented) The method according to claim 1, wherein the organic solvent having a boiling point lower than that of water is immiscible with water, and the organic solvent having a boiling point lower than that of water is evaporated from an emulsion in the microsphere storage tank by warming, pressure reduction, blowing of a gas, evaporation with a hollow fiber membrane module, or a combination of these methods.

6. (Original) The method according to claim 5, wherein the organic solvent having a boiling point lower than that of water is evaporated from an emulsion in the microsphere storage tank by evaporation with a hollow fiber membrane module.

7. (Original) The method according to claim 6, wherein the organic solvent having a boiling point lower than that of water is a halogenated aliphatic hydrocarbon solvent.

8. (Currently Amended) The method according to claim 1, wherein the organic solvent having a boiling point lower than that of water is miscible with water, and the evaporation of the organic solvent having a boiling point lower than that of water from an emulsion in a microsphere storage tank in step (d-1)ii) or step (d-2)ii) is not carried out.

9. (Original) The method according to claim 8, wherein the organic solvent having a boiling point lower than that of water is a water-miscible ketone solvent.

10. (Original) The method according to claim 8, wherein the medicament-containing polymer solution is one in which a medicament is suspended and a biocompatible and biodegradable hardly-water-soluble polymer is dissolved in a water-miscible organic solvent having a boiling point lower than that of water, and the aqueous solution is a uniform aqueous solution containing a solvent being immiscible with said water-miscible organic solvent but being miscible with water.

11. (Currently Amended) The method according to claim 1, wherein during **[[Step]]** step (d-1) or **[[Step]]** step (d-2), the filtration speed through the cross flow filter and the influx speed of the emulsion from the emulsifying device into the microsphere

storage tank are controlled substantially the same so as to keep the volume of the emulsion in said tank substantially constant.

12. (Currently amended) The method according to claim 4, wherein the capacity of the microsphere storage tank is 10 to 1000 times of that of the emulsifying device for batch-treatment.

13. (Currently Amended) The method according to claim 1, wherein the pore size of ~~[[the]]~~ a membrane filter of the cross flow filter is in the range of 1/300 to 1/3 of the average particle size of the desired ~~microsphere~~ microspheres, and the filtration speed of the filtrate from the cross flow filter is adjusted to the range of 1/100 to 1/3 of the introduction speed of the emulsion into said cross flow filter.

14. (Original) The method according to claim 13, wherein the pore size of the membrane filter of the cross flow filter is within the range of 0.01 to 10 μm .

15. (Currently Amended) The method according to claim 1, wherein the ~~emulsification~~ emulsifying step (a) is carried out ~~[[by]]~~ with a high-speed rotary homogenizer utilizing inner shear (liquid-liquid shear).

16. (Currently Amended) The method according to claim 1, wherein the ~~emulsification in Step~~ emulsifying step (a) is carried out using the aqueous solution in a volume of 1 to 1000 times of that of the medicament-containing polymer solution.

17. (Currently amended) The method according to claim 1, wherein **[[Step]]** step (d-1) is employed.

18. (Currently amended) The method according to claim 1, wherein **[[Step]]** step (d-2) is employed.

19. (Original) The method according to any one of claims 1 to 18, wherein the biocompatible and biodegradable hardly-water-soluble polymer is a polyester of hydroxyfatty acid.

20. (Previously presented) The method according to claim 1, wherein the microspheres are collected by dead-end filtration, cross flow filtration or centrifugation, or a combination of these methods.

21. (Original) The method according to claim 17, wherein the medicament is recovered from the aqueous solution after the collection of the microspheres.

22. (Currently Amended) A method for preparation of lyophilized ~~microsphere~~ microspheres, which comprises preparing microspheres by the method as set forth in claim 1, dispersing the microspheres thus obtained in an aqueous solution of an excipient if necessary, and then subjecting the resultant to lyophilization.

23-31. (Cancelled).